REMARKS

Amended claims 8, 12-17, and 19 are pending in the application. Claim 18 has been cancelled.

35 U.S.C. §112, FIRST PARAGRAPH REJECTION OF CLAIMS 8, 12-17 AND 19

The Examiner has rejected claims 8 and 12-19 under 35 U.S.C. §112, first paragraph, on the grounds that they describe a process for which neither the time nor the conditions to achieve the intended result are disclosed by the specification. The Examiner has suggested amending these claims to include the phrase " . . . for a time and under conditions effective to inhibit picornaviral replication" in order to overcome the 35 U.S.C. §112, first paragraph rejections. In Example 6 on page 34, methods of treatment with compounds of the present invention are disclosed. The example ends with the sentence "Preferably, the compositions are administered until a defined endpoint is reached, such as the absence of a particular virus, reduction or absence of symptoms of a disease caused by the virus, or prevention of infection of the subject by the virus." As evidenced, the specification indeed discloses multiple potential intended results and the time and conditions necessary (the instructions to administering the compound in a clinical setting) for each intended result can readily be determined by a person skilled in the art. For these reasons, Applicants have amended claims 8, 13-17, and 19 by adding the phrase "to effectively inhibit picornaviral replication" to comply with the Examiner's position that a method claim ought to end with the intended result stated. Applicants believe that because of its dependence on claim 8, claim 12 need not be amended to include this language. Applicants respectfully request that the Examiner withdraw his 35 U.S.C. §112, first paragraph rejections regarding this issue for claims 8, 13-17, and 19.

Additionally, the Examiner has rejected claims 8 and 12-19 under 35 U.S.C. §112, first paragraph on the grounds that they contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors possessed the claimed invention. In previous claims 8 and 18, it was recited that Y and Y′

can be hydroxyl, but the Examiner did not find support for this identification in the specification. On page 30, Table I in the specification Y′ can be hydroxyl. Additionally, originally filed claim 5 also recites hydroxyl as a substituent for Y′. Therefore, Applicants have canceled claim 18 and amended claim 8, 17, and 19 to recite that Y′ can be hydroxyl. The Examiner noted that in claims 17 and 19 the phrase "which includes the use of" is utilized although the Examiner did not find support for this phrase in the specification. Claims 17 and 19 have been amended to delete this phrase and insert instead "comprising." Support for the use of "comprising" can be found on page 34, lines 10-24 of the specification. Furthermore, the Examiner noted that in claims 18 and 19 it is recited that Y and Y′ cannot by hydrogen simultaneously, although the Examiner did not find support for this detail in the specification. Claim 19 has been amended to remove this language and claim 18 has been canceled because without this language its content was duplicative of claim 8.

Yet again, the Examiner rejected claims 8 and 12-19 under 35 U.S.C. §112, second paragraph, for failing to point out and distinctly claim what the Applicants believe to be their invention. Applicants have amended claims 8, 13-17, and 19 to adopt the Examiner's suggested language to better describe "an effective amount." Additionally, Applicants note that "a subject" as recited in the claims of the instant application refer to an animate being and postulate that no one skilled in the art would think of a test tube as "a subject." The Applicants respectfully request the Examiner to reconsider this language where the method of inhibiting picornaviral replication comprises administering an effective amount of the claimed compound to the subject.

The Examiner objected to the indefinite language of "having substantially similar binding properties as the oligopeptide" in claims 8 and 17-19 because the binding properties are not further defined. Applicants have amended claims 8, 17, and 19 to overcome the Examiner's objection by deleting such language. As stated above, the Examiner objected to the phrase "includes the use" in claims 17 and 19 because the process steps are then indefinite. Applicants have amended claims 17 and 19 to recite instead "comprises."

The Examiner also objected to claims 8, 17, and 19 because they recite Y and Y′ as a "keto, carbamido, sulfoxide, alkylsulfonyl, and sulfone." The Examiner objected to these

limitations because they are functional groups having only one bonding group disclosed. By taking this position of indefiniteness, the Examiner is indirectly requiring the Applicants to disclose numerous species of these functional groups in the specification. However, patent law does not require an applicant to disclose every species encompassed in a claim, even in an upredictable art. *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976). The Court in *Angstadt* further noted that:

> "To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed."

Id.

Moreover, the Board of Patent Appeals and Interferences found it improper for an examiner to reject claims based on terms such as alkyl, alkoxy, alkylene, and divalent hydrocarbon radicals as indefinite when such terms are not broader than those provided in the specification. *Ex parte Altermatt*, 183 USPQ 46 (BPAI 1974). In this instance, the Applicants' limitations are exactly like those provided in the original specification because the Applicants original claim 8, which includes these limitations, is part of the original specification. Further support for these limitations can be found on page 5, lines 10-11. Additionally, Applicants amended the typographical error in "carbamido" in claims 8, 17, 19 to "carbamide," which has the defined structure of NH_2CONH_2. For these reasons, Applicants consider the language "keto, carbamide, sulfoxide, alkylsulfonyl, and sulfone" to be definite.

Applicants have further amended claims 13 and 14 to correct a typographical error involving hyphens. Additionally, the Examiner noted a typographical error in claim 13 where the prime symbol did not follow the symbol Z. Applicants have also corrected this error.

The Examiner has suggested moving the phrase "or alternatively Z′ and R1 collectively form a ring" so that it precedes the definitions of Y and Y′. Applicants have responded positively to the Examiner's suggestion. The Examiner noted that the position of the chemical formula in claim 15 should be altered to follow the phrase "has the formula." Applicants have again responded favorably to the Examiner's suggestion of placing the chemical formula behind the phrase.

Lastly, the Examiner requested that "wherein" should be present before the definition of X in claim 17. Applicants have fulfilled the Examiner's request.

35 U.S.C. §102 (b), SECOND PARAGRAPH REJECTION OF CLAIMS 8 AND 12-19

The Examiner rejected claims 8 and 18 under 35 U.S.C. §102(b) as being anticipated by Berger, U.S. Patent 3,657,436 (the '436 patent). Under the same statute, the Examiner rejected claims 8, 12, 14, and 17-19 as being anticipated by Baratz, U.S. Patent 4,333,941 (the '941 patent). Lastly, the Examiner rejected claims 8 and 18 under 35 U.S.C. §102(b) as being anticipated by Singh, et al. (Tetrahedron Letters 1991 32:5279-5282). The following arguments will demonstrate how Applicants' compounds described in the amended claims herein differs from the compounds of the prior art.

Berger, U.S. Patent 3,657,436

The Examiner rejected claims 8 and 18 under 35 U.S.C. §102(b) as being anticipated by Berger, U.S. Patent 3,657,436 (the '436 patent). Applicants have canceled claim 18 and amended claims 8, 17, and 19 to remove the possibility of Z being NH_2. Applicants believe that the compounds referenced in the '436 patent do not anticipate the compounds of the instant application. In Table I (at page 15 of this Amendment), the generic compound formulae are provided. Substituents for each formula were chosen to correspond to produce identical compounds. As can be seen, because Z cannot be NH_2, the '436 patent does not anticipate Applicants' compounds regardless of the identity of other substituents chosen. For this reason, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejection of claim 8.

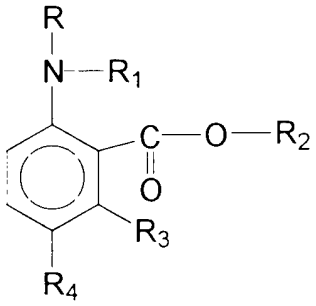
Baratz, U.S. Patent 4,333,941

Next, the Examiner rejected claims 8, 12, 14, and 17-19 under 35 U.S.C. §102(b) as being anticipated by Baratz, U.S. Patent 4,333,941 (the '941 patent). Claims 8, 17, and 19 were amended to remove the possibility of R^{14} being a lower alkyl. In Table II (at page 16 of this Amendment), substituents were chosen in order to compare the compounds of the '941 patent to that of the instant application. In order to make this comparison, the generic formulae for each compound class is listed with allowed substituents chosen to produce identical compounds. Table II demonstrates that when variables are chosen in Applicants's formula to correspond to the '941 patent, it is impossible to achieve the '941 compound because R^{14} is not a lower alkyl in the newly amended claims. Additionally, Applicants canceled claim 18. Therefore, Applicants believe that the '941 compound does not anticipate the claims as amended. For this reason, Applicants respectfully request that the Examiner withdraw this 35 U.S.C. §102(b) rejections of claims 8, 12, 14, and 17-19.

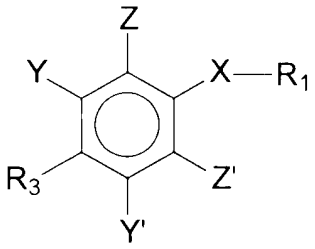
Singh, Tetrahedron Letters 32:5279-5282 (1991)

Finally, the Examiner rejected claims 8 and 18 under 35 U.S.C. §102(b) as being anticipated by Singh, et al. Tetrahedron Letters 32:5279-5282 (1991) (Singh). Applicants respectfully disagree with the Examiner regarding this rejection. In Table III (also at page 16 of this Amendment), the Examiner will see that Singh, et al.'s thysanone cannot anticipate the compounds of the instant application because the allowed substituents do not correspond. Substituents cannot be chosen for Applicants's formula that yield the Singh compounds because R^{11} cannot be a heterocyclic ring. Thus, it is impossible to create thysanone given the required substitutents. For this reason, Applicants respectfully request the Examiner to withdraw this 35 U.S.C. §102(b) rejection of claim 8. Applicants have canceled claim 18.

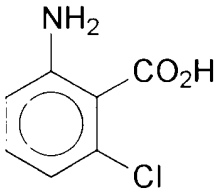
Table I. Comparison of the Compounds in the '436 Patent and Instant Application



Berger's compound formula
When the following substituents from claim 1 are chosen:
R=H
R_1=H
R_2=H
R_3=H or Cl
R_4=H or Cl



Applicants' compound formula
When the following substituents from claim 8 are chosen:
Z= not amino
X=C=O
R_1=OH
Z'=Cl
Y'=H
R_3=H
Y=H



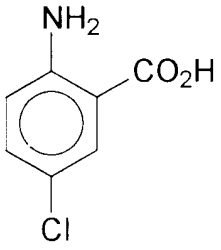
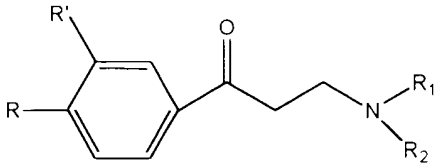
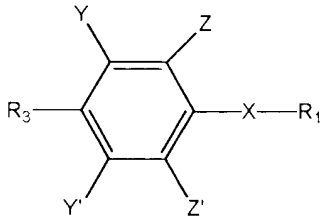


Table II Comparision of the Compounds in the '941 Patent and Instant Application

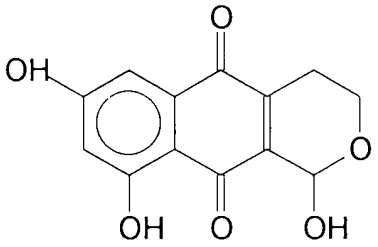


Baratz's compound formula
When the following substituents from claim 1 are chosen:
R'=H, halogen
R=H, halo, 1-12 alkoxy
R_1 and R_2=lower alkyl, with the N a heterocyclic amino group or N-alkyl quaternary heterocyclic ammonium group of 4-6 C and up to 1 additional hetero atom (O, S, N), triloweralkylammonium

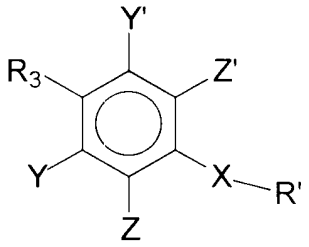


Applicants' compound formula
When the following substituents from claims 8 are chosen:
X=C=O
R_1=2 C hydrocarbon chain and R^{11}
R^{11}=$NR^{13}R^{14}$
R^{13}=lower alkyl
R^{14}=cannot be lower alkyl or other R_1 or R_2 substituents from the '941 patent
Z'=H
Y'=H
R_3=H
Y=halogen
Z=H

Table III. Comparison of the Compounds from Singh and Instant Application



Thysanone

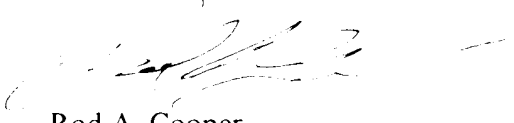


Applicants' compound formula
When the following substituents from claim 8 are chosen:
X=C=O
R_1 and Z' form a C_6 unsaturated ring system which may be additionally substituted with R^{11}, a keto;
Z=OH
Y=H
R_3=OH
Y=H

CONCLUSION

For reasons delineated above, Applicants respectfully request the consideration of all pending claims, and favorable action on the same.

Respectfully submitted,

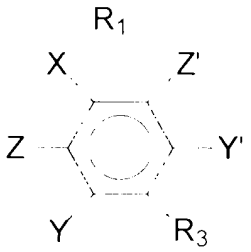


Rod A. Cooper
Registration No. 42,436

RAC/aep
September 17, 2001
SIDLEY, AUSTIN, BROWN & WOOD
717 N. Harwood
Suite 3400
Dallas, Texas 75202
(214) 981-3331

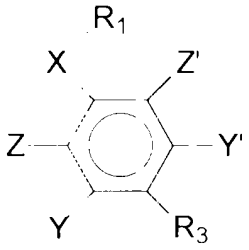
APPENDIX DEMONSTRATING AMENDMENTS

ABSTRACT



A compound having the formula (I) wherein the substituents are defined herein. Also provided are pharmaceutical compositions including a compound of formula (I) in a pharmaceutical carrier, for treating a disease caused by a picornavirus. Also provided is a method of treating a subject with a disease caused by a picornavirus, including a compound of formula (I) in a pharmaceutical carrier

8. (Thrice Amended) A method of inhibiting picornaviral replication in a subject, comprising the step of administering an effective amount of a compound having a formula:



wherein

X is selected from the group consisting of C=O, S=O, C=S, (C=O)-NH, (C=O)-O and (C=O)-S;

R_1 is selected from the group consisting of:

(i) hydrogen, hydroxyl or a hydrocarbon chain from 1 to about 10 carbons long selected from the group consisting of saturated, unsaturated and fluorinated, wherein said

hydrocarbon chain is unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, CO_2R^{13}, $O(C{=}OR^{13})$, SO_2R^{14}, SOR^{14}, $(C{=}O)NR^{13}R^{14}$, or $NR^{14}(C{=}O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, [C_1-C_4 alkyl] and benzyl;

(ii) an oligopeptide or peptidomimetic molecule of 1 to 5 amino acids [or a peptidomimetic molecule having substantially similar binding properties as the oligopeptide];

(iii) C_3-C_6 cycloalkyl, C_6-C_{10} bicycloalkyl, C_3-C_7 cycloalkylmethyl, or C_7-C_{10} arylalkyl, which may be additionally substituted with R^{11} as defined above;

R_3 is selected from the group consisting of:

(i) hydrogen, phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain or O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids[, an oligopeptide of 1 to 3 amino acids] joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, [amino,] carboxyl and NHR^{11}, wherein R^{11} is defined as above;

Z' is selected from the group consisting of:

(i) hydroxyl, amino,carbamido, carbamyl, carbamyloxy or halogen;

(ii) hydrogen, and

(iii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl, or $C_{1[,]}$-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

alternatively Z' and R_1 collectively form a ring system selected from the group consisting of:

(a) C_5-C_8 carbocyclic ring which may be saturated or unsaturated, and which may be additionally substituted with at least one R^{11} as defined above; and

(b) C_5-C_{10} heterocyclic ring system which may be saturated or unsaturated and which includes at least one nitrogen, oxygen or sulfur atom, and which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydrogen, [hydroxy,] halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, [carbamido] carbamide, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, or sulfone; [and]

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; [and]

(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids[or a peptidomimetic]; and

(v) Y' may additionally be hydroxyl;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen;
[alternatively Z' and R_1 collectively form a ring system selected from the group consisting of:

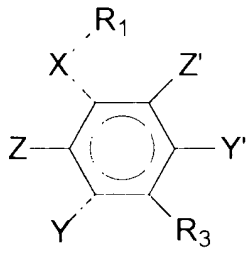
(a) C_5-C_8 carbocyclic ring which may be saturated or unsaturated, and which may be additionally substituted with at least one R^{11} as defined above; and

(b) C_5-C_{10} heterocyclic ring system which may be saturated or unsaturated and which includes at least one nitrogen, oxygen or sulfur atom, and which may be additionally substituted with at least one R^{11} as defined above;]

to effectively inhibit picornaviral replication.

12. (Twice Amended) A method according to claim 8, wherein the picornavirus species is a rhinovirus [species].

13. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:



wherein X is –C=O;

R_1 is $-CF_3$;

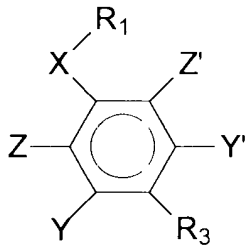
Z and Z′ are hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

R_3 is hydrogen; and

Y and Y′ are selected from the group consisting of –Cl, –I, –Br, $-CF_3$, –F, –CN, [-] COOH, $-SO_3H$, $-SO_2NH_2$ and $-CONH_2$

to effectively inhibit picornaviral replication.

14. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:



wherein X is –C=O;

R_1 is $-CF_3$;

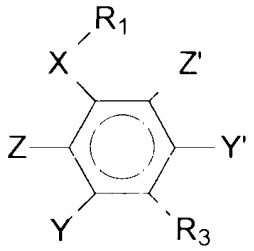
Z is hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

Z′ and R_3 are hydrogen; and

Y and Y′ are selected from the group consisting of –Cl, –I, –Br, $-CF_3$, –F, –CN, –COOH, $-SO_3H$, $-SO_2NH_2$ and $-CONH_2$

to effectively inhibit picornaviral replication.

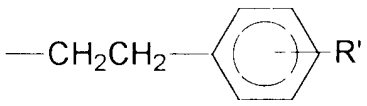
15. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:

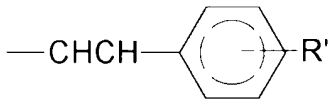


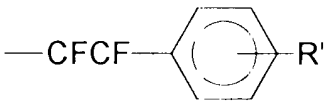
[has the formula]

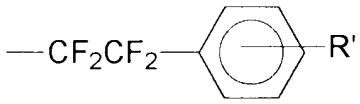
wherein X is –C=O;

R_1 is H, $-CH_3$, $-CF_3$, $CH_3-CH_2-CH_2-CH_2-CH_2-$, CH_3-CH_2-, $CH_3-CH_2-CH_2-$, $CF_3-CF_2-CF_2-CF_2-CF_2-$, –NH–R′′or one of the following phenyl groups









wherein R′ is –OH, $-NH_2$, –COOH, or $-COCH_3$ and R′′ is –OH, $-NH_2$, $-OCH_3$ [and] or $-OCH_2CH_3$;

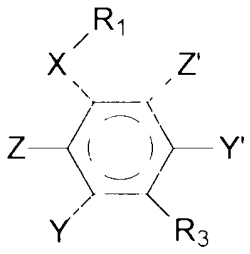
Z and Z′ are hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

R_3 is hydrogen; and

Y and Y′ are $-CF_3$

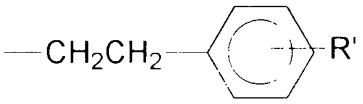
to effectively inhibit picornaviral replication.

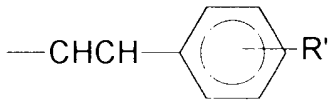
16. (Thrice Amended) A method for inhibiting picornaviral replication in a subject, wherein said compound has the formula:

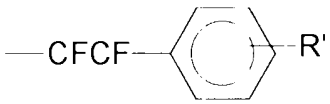


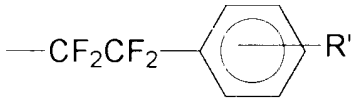
wherein X is –C=O;

R_1 is H, $-CH_3$, $-CF_3$, $CH_3-CH_2-CH_2-CH_2-CH_2-$, CH_3-CH_2-, $CH_3-CH_2-CH_2-$, $CF_3-CF_2-CF_2-CF_2-CF_2-$, –NH–R′′, or one of the following phenyl groups









wherein R′ is –OH, $-NH_2$, –COOH, or $-COCH_3$ and R′′ is –OH, $-NH_2$, $-OCH_3$ and $-OCH_2CH_3$;

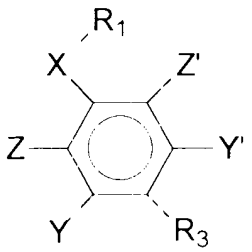
Z is hydroxyl, except when X-R_1 is a fluorinated keto acyl group, Z must be hydrogen;

Z′ and R_3 are hydrogen, and

Y and Y′ are $-CF_3$

to effectively inhibit picornaviral replication.

17. (Twice Amended) A method of inhibiting picornaviral replication in a subject, wherein said method comprises [includes] the use of a compound with the formula:



wherein X is selected from the group consisting of –C=O-, -S=O-, and -C=S-;

R_1 is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, COR^{13}, $O(C{=}OR^{13})$, SO_2R^{14}, SOR^{14}, $(C{=}O)NR^{13}R^{14}$, or $NR^{14}(C{=}O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl, and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, [C_1-C_4 alkyl] and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain and O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide or a peptidomimetic molecule of 1 to 3 amino acids, [an oligopeptide of 1 to 3 amino acids] joined to the backbone by an oxygen [or a peptidomimetic];

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, [amino,] carboxyl, and NHR^{11}, wherein R^{11} is defined as above;

Z′ is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy, and halogen;

(ii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl and C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) hydrogen, [hydroxy,] halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, [carbamido] carbamide, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, or sulfone; [and]

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; [and]

(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids[or a peptidomimetic]; and

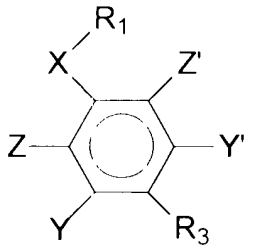
(v) Y' may additionally be hydroxyl;

(iv) an oligopeptide of 1 to 3 amino acids or a peptidomimetic;

and pharmaceutically acceptable salts thereof; with the proviso that when X-R_1 is a fluorinated keto acyl, Z is hydrogen

to effectively inhibit picornaviral replication.

19. (Once Amended) A method of inhibiting picornaviral replication in a subject, wherein said method comprises [includes] the use of a compound with the formula:



wherein X is selected from the group consisting of –C=O-, -S=O-, and -C=S-;

R_1 is selected from the group consisting of:

(i) a hydrocarbon chain which may be unsubstituted or substituted with at least one R^{11}, wherein R^{11} is selected from the group consisting of:

(ia) C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_6-C_{10} bicycloalkyl or aryl which may be substituted or unsubstituted;

(ib) halogen, cyano, nitro, amino, hydroxy, adamantyl, carbamyl, carbamyloxy or keto;

(ic) an oligopeptide of 1-3 amino acid residues; and

(id) $NR^{13}R^{14}$, COR^{13}, $O(C{=}OR^{13})$, SO_2R^{14}, SOR^{14}, $(C{=}O)NR^{13}R^{14}$, or $NR^{14}(C{=}O)R^{13}$;

wherein:

R^{13} is selected from the group consisting of hydrogen, phenyl, benzyl, C_1-C_6 alkyl, and C_3-C_6 alkoxyalkyl; and

R^{14} is selected from the group consisting of hydrogen, hydroxyl, [C_1-C_4 alkyl] and benzyl;

R_3 is selected from the group consisting of:

(i) phenyl, hydroxyl, C_1-C_{12} hydrocarbon chain and O-C_1-C_{12} hydrocarbon chain which may be additionally substituted with at least one R^{11} as defined above; and

(ii) an oligopeptide of 1 to 3 amino acids[, an oligopeptide of 1 to 3 amino acids] joined to the backbone by an oxygen or a peptidomimetic;

Z is selected from the group consisting of hydrogen, hydroxyl, sulfhydryl, [amino,] carboxyl, and NHR^{11}, wherein R^{11} is defined as above;

Z′ is selected from the group consisting of:

(i) hydroxyl, amino, carbamido, carbamyl, carbamyloxy, and halogen;

(ii) C_1-C_4 alkyl, C_1-C_4 alkenyl, C_3-C_7 cycloalkenyl and C_1-C_3 alkoxy which may be additionally substituted with at least one R^{11} as defined above;

Y and Y' are independently selected from the group consisting of:

(i) <u>hydrogen</u>, [hydroxy,] halogen, C_1-C_4 haloalkyl, or C_1-C_4 haloalkoxy;

(ii) carbamyl, [carbamido] <u>carbamide</u>, cyano, keto, vinyl, sulfoxide, nitro, C_1-C_3 alkylsulfonyl, or sulfone; [and]

(iii) C_1-C_3 alkyl which may be additionally substituted with at least one R^{11} as defined above; [and]

(iv) an oligopeptide or a peptidomimetic of 1 to 3 amino acids[or a peptidomimetic]; and

(v) Y' may additionally be hydroxyl;

and pharmaceutically acceptable salts thereof; with the proviso that when $X\text{-}R_1$ is a fluorinated keto acyl, Z is hydrogen;[.]

to effectively inhibit picornaviral replication.